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The New Pap Smear Guidelines

Teaching Old Dogs New Tricks

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Objectives

- Discuss the history of Pap Smears
- Review USPSTF Guidelines for Pap smears
- Articulate the evidence behind USPSTF Guidelines
- Distinguish how to use ASCCP algorithms to determine follow up of Pap results

History of Pap Smears

1928

George Papanicolaou, and his devoted wife, Andromache Mavroyenous

The Papanicolaou smear, first reported in 1928

1941

Efficacy was proved by 1941

20th
Century

Most significant advance in the control of cancer in the 20th century.

Cancer of the cervix follows a predictable sequence.

- Precancerous changes
- Evolution from the precancerous stage to cancer is slow

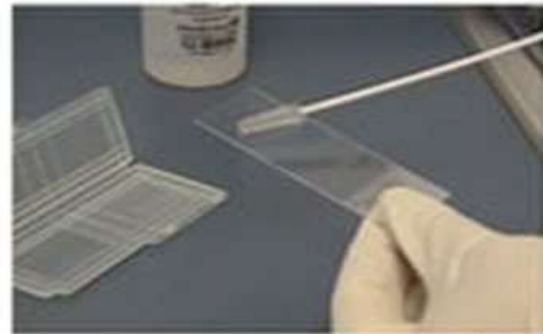
- Annual screening makes this a curable cancer and totally preventable disease

History of Pap Smears

Make Pap Smear



- As thin as possible
- Properly labeled



- 95% Ethanol.
- 95% Rectified Spirit.
- 100% Methanol.
- 80% Isopropanol or Propanol.
- Ether/95% Ethanol (1: 1).
- Spray fixatives contains isopropanol and propylene glycol.



Figure 5.4. Spray fixation of smears. The optimal distance between the nozzle of the spray can and the slide is approximately 10 inches (30 cm).

Immediate fixation (within seconds) is critical in order to prevent air-drying artifact

Evolution of Pap Smears

Liquid Based Cytology

(ThinPrep®), First
Liquid Based Pap
Test May 1996

BD SurePath™

Addition of HPV
testing

Now able to test
HPV, GC,
Chlamydia, Trich



Evolution of Liquid Based Pap

Red blood cells
and some
leukocytes are
eliminated by
density
centrifugation

Evenly distributed
deposit of cells in
13mm diameter

Final staining step
that discretely stains
individual slides



Advantage of Liquid-Based Pap



Pap Smear Nomenclature

BETHESDA SYSTEM 2001 FOR REPORTING PAP RESULTS

- 8,000 -12,000 cells for slide based pap
- 5,000 cells for Liquid based

FIVE COMPONENTS OF A PAP SMEAR REPORT

1. Adequacy: satisfactory vs unsatisfactory
2. General category: negative for intraepithelial lesions vs epithelial cell abnormality
3. Non-neoplastic results/ organisms: Trich, Fungal, Bacterial vaginosis, Bacteria associated with actinomyces, cellular changes associated with HSV
4. Other Non-neoplastic findings:
 - a. Reactive cellular changes due to Infection, radiation, IUD
 - b. Benign glandular cells after hysterectomy
 - c. Atrophy
5. Interpretation

Pap Smear Nomenclature

Interpretation

SQUAMOUS CELL ABNORMALITY

- Atypical squamous cells
- of undetermined significance (ASC-US)
- Cannot rule out HGSIL (ASC-H)
- Low Grade Squamous Epithelial Lesions (LGSIL)
- High Grade Squamous Epithelial Lesions (HGSIL)
- Squamous Cell Carcinoma

GLANDULAR CELL ABNORMALITY

- Atypical Glandular cells (AGC) (specify endocervical, endometrial, or not specified)
- Atypical Glandular cells, favor neoplastic (specify endocervical, endometrial, or not specified)
- Endocervical adenocarcinoma in situ (AIS)
- Adenocarcinoma (endocervical/ endometrial/ extrauterine or not specified)

Poll Question

17 year old comes in to your office seeking birth control as she has recently become sexually active. Your recommendation for pap smear screening is:

- A: Pap smear yearly with HPV testing at age 21
- B: Pap smear now since she is sexually active
- C: Pap smear every three years starting at age 21
- D: Pap smear every with HPV testing five years starting at age 21

Previous Practice

Pap every year, starting as soon as sexually active

Follow up abnormal pap smear with colposcopy

If colposcopy abnormal, do LEEP/ Cryotherapy/
Laser

Assessment of Risk

High-risk HPV infection is associated with nearly all cases of cervical cancer

Women are exposed to hrHPV through sexual intercourse

A large proportion of HPV infections resolve spontaneously

USPSTF Guidelines

August 2018

Grade A recommendation

WOMEN AGED 21 TO 29 YEARS	WOMEN AGED 30 TO 65 YEARS
<ul style="list-style-type: none">• Screening every 3 years with cervical cytology alone	<ul style="list-style-type: none">• Screening every 3 years with cervical cytology alone• Every 5 years with high-risk human papillomavirus (hrHPV) testing alone• Every 5 years with hrHPV testing in combination with cytology (co-testing)

USPSTF Guidelines

August 20 18

Grade D recommendation

WOMEN YOUNGER THAN 21 YEARS	WOMEN WHO HAVE HAD A HYSTERECTOMY	Women older than 65 years
<ul style="list-style-type: none">• Recommends against screening for cervical cancer in women younger than 21 years	<ul style="list-style-type: none">• Recommends against screening if hysterectomy with removal of the cervix and no history of a high-grade precancerous lesion (ie, CIN2 or 3) or cervical cancer	<ul style="list-style-type: none">• Recommends against screening in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer

Women Younger Than 21 Years

Cervical cancer is rare before age 21 years

Exposure of cervical cells to hrHPV during vaginal intercourse may lead to cervical carcinogenesis

The process has multiple steps, involves regression, and is generally not rapid

Evidence suggests that screening earlier than age 21 years, regardless of sexual history, would lead to more harm than benefit

Treatment of CIN 2 or CIN 3 among women younger than 21 years may increase risk for adverse pregnancy outcomes

Women Older Than 65 Years

American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology (ACS/ASCCP/ASCP)

define adequate prior screening

- 3 consecutive negative cytology results
- 2 consecutive negative co-testing results
 - Within 10 years before stopping screening
 - Most recent test occurring within 5 years

Continue routine screening even if this extends past age 65

- At least 20 years after spontaneous regression
- Appropriate management of a precancerous lesion

Once screening has stopped do not resume in women older than 65 years, even if they report having a new sexual partner

Women Older Than 65 Years Who Have Not Been Adequately Screened

One-fourth of women aged 45 to 64 years have not been screened for cervical cancer in the preceding 3 years

- Limited access to care
- Racial/ethnic minority groups
- Countries where screening is not available

Screening in women older than 65 years who are otherwise at high risk

- History of high-grade precancerous lesions or cervical cancer
 - In utero exposure to diethylstilbestrol
 - Compromised immune system

USPSTF Guidelines

- Recommendations apply to all asymptomatic individuals with a cervix, regardless of their sexual history
- Does not apply to:
 - Women who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer
 - Women with in utero exposure to diethylstilbestrol
 - Women who have a compromised immune system (eg, women living with HIV)

USPSTF Guidelines

- Current evidence: no clinically important differences between liquid-based cytology and conventional cytology
- hrHPV testing has been used for:
 - Primary screening
 - Co-testing with cytology
 - Follow-up testing of positive cytology results (reflex hrHPV)

USPSTF Screening Guidelines

Cytology alone is slightly less sensitive for detecting CIN 2 and CIN 3 than screening with hrHPV testing alone

Cytology alone, hrHPV testing alone, and both in combination offer a reasonable balance between benefits and harms for women aged 30 to 65 years

hrHPV testing alone or in combination with cytology detects more cases of CIN 2 and CIN 3, thus results in more diagnostic colposcopies for each case detected

Protocols for Triage of Abnormal Pap

Different protocols (ASCCP most common)

Generally similar detection rates for CIN 2 and CIN 3

Proceeding directly to diagnostic colposcopy leads to greater number of colposcopies

Must adhere to protocols to maintaining comparable benefits and harms of screening with cytology alone or hrHPV testing alone

Screening Interval

SCREENING MORE FREQUENTLY THAN EVERY 3 YEARS WITH CYTOLOGY ALONE

- Confers little additional benefit, with a large increase in harms
- Additional procedures and assessment
- Treatment of transient lesions
 - Can lead to procedures with unwanted adverse effects
 - Cervical incompetence and preterm labor during pregnancy

5-YEAR SCREENING INTERVAL FOR PRIMARY HRHPV TESTING ALONE OR COTESTING OFFERS THE BEST BALANCE OF BENEFITS AND HARMS

- More frequent does not substantially improve benefit but significantly increases the number of screening tests and colposcopies

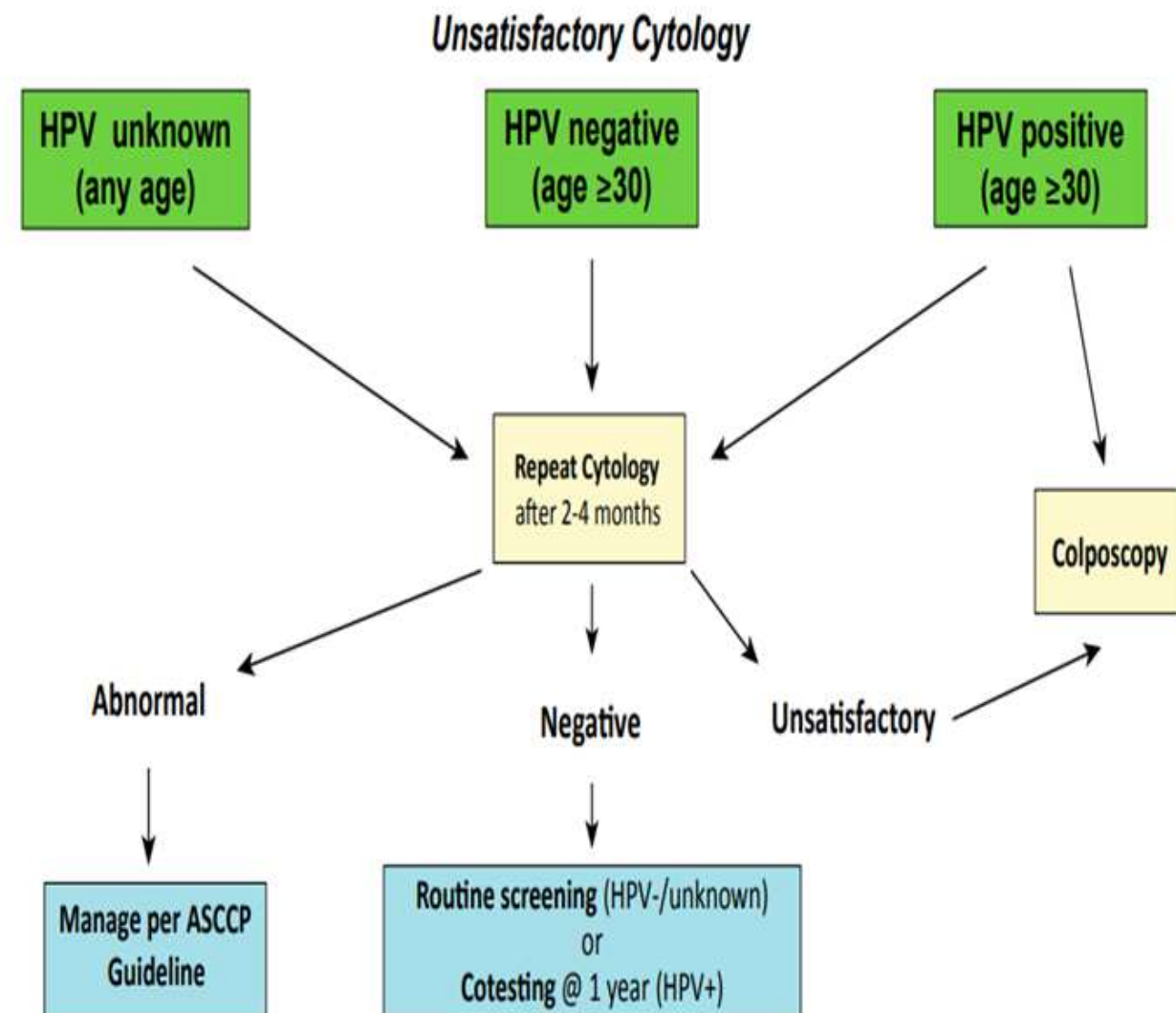
Poll Question

24 year old comes in for annual exam. Her pap shows LgSIL. She had normal cytology on her first pap 3 years ago. Your recommendation for follow up:

- A: Colposcopy
- B: Repeat Pap smear in 1 year
- C: LEEP/Cryo
- D: Repeat Pap smear with HPV testing now

ASCCP Guidelines

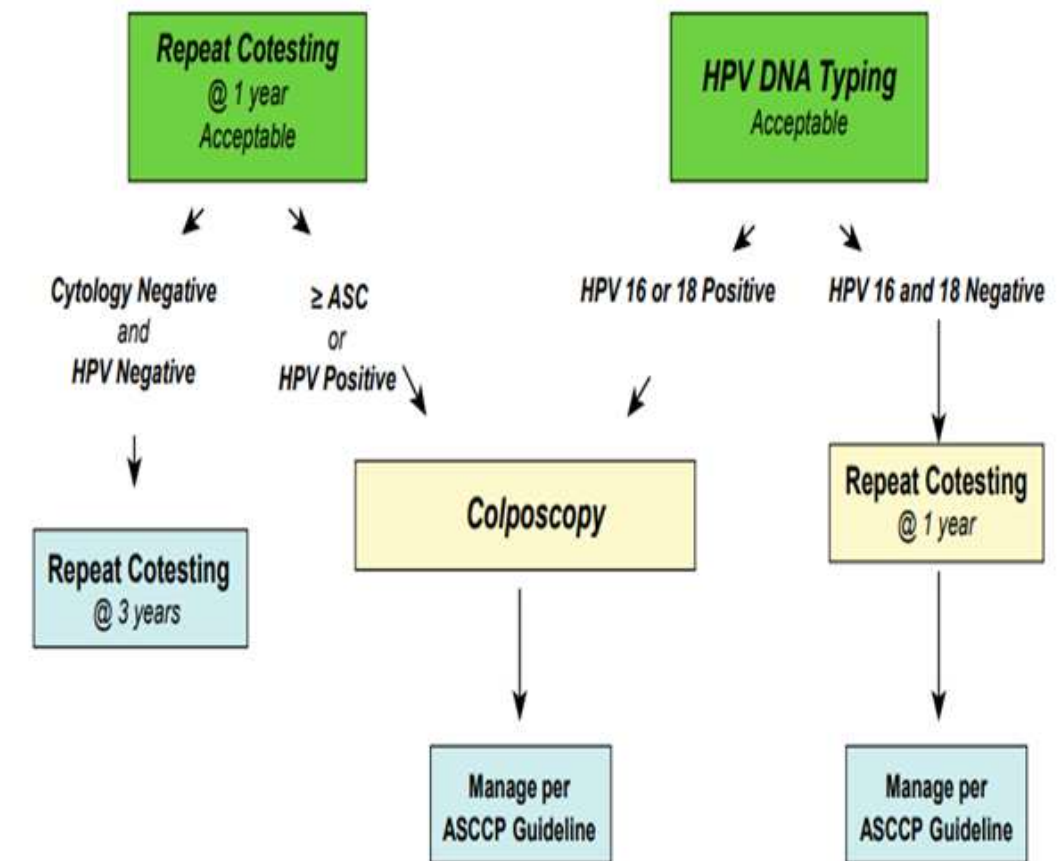
Unsatisfactory Cytology



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Normal Cytology/HPV Positive

Management of Women \geq Age 30, who are Cytology Negative, but HPV Positive




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The ASCCP Management Guidelines App & Web Application is Now Available

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★★★★★ Years Old Medical Amer

What's New [Version History](#)

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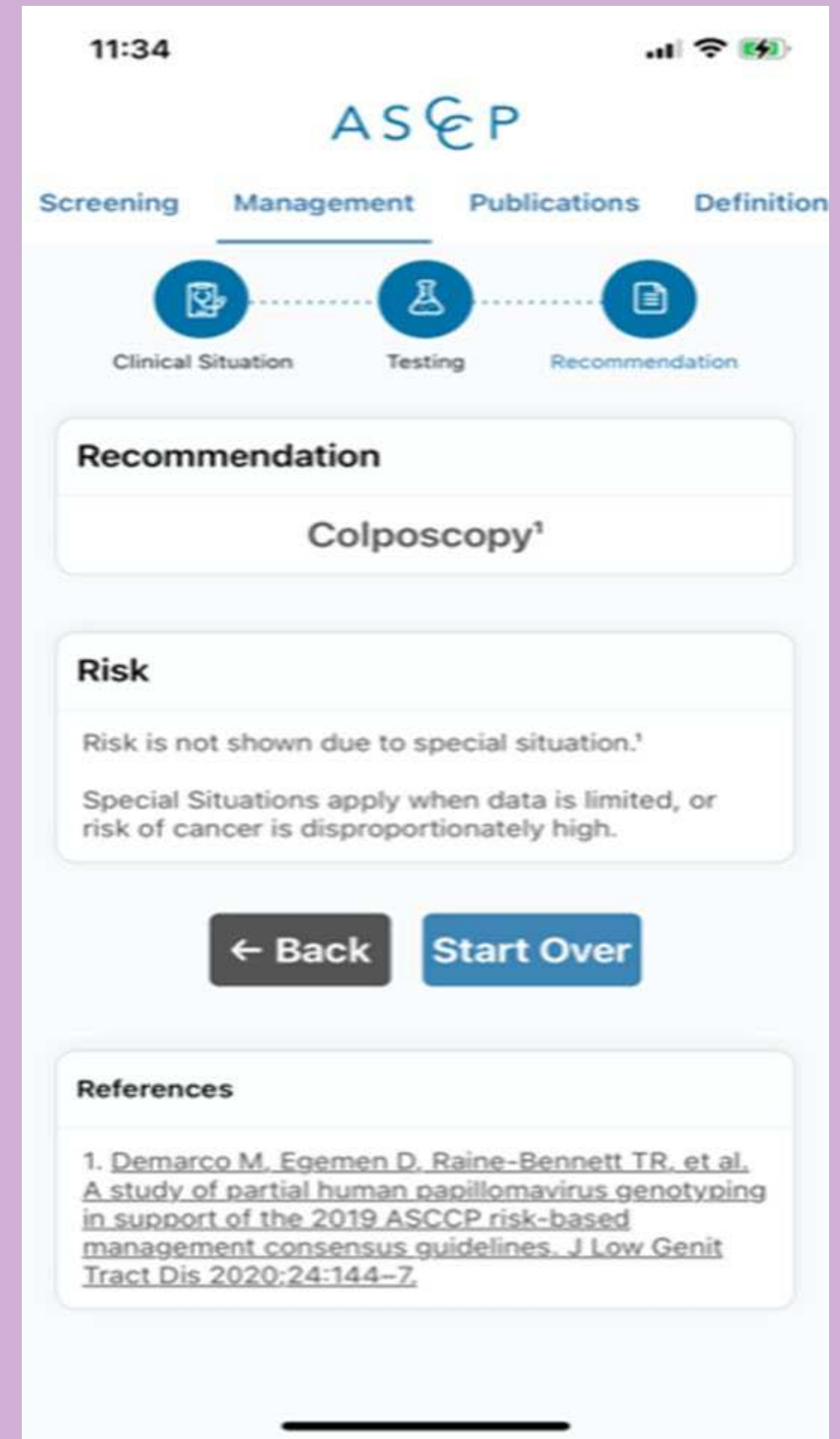
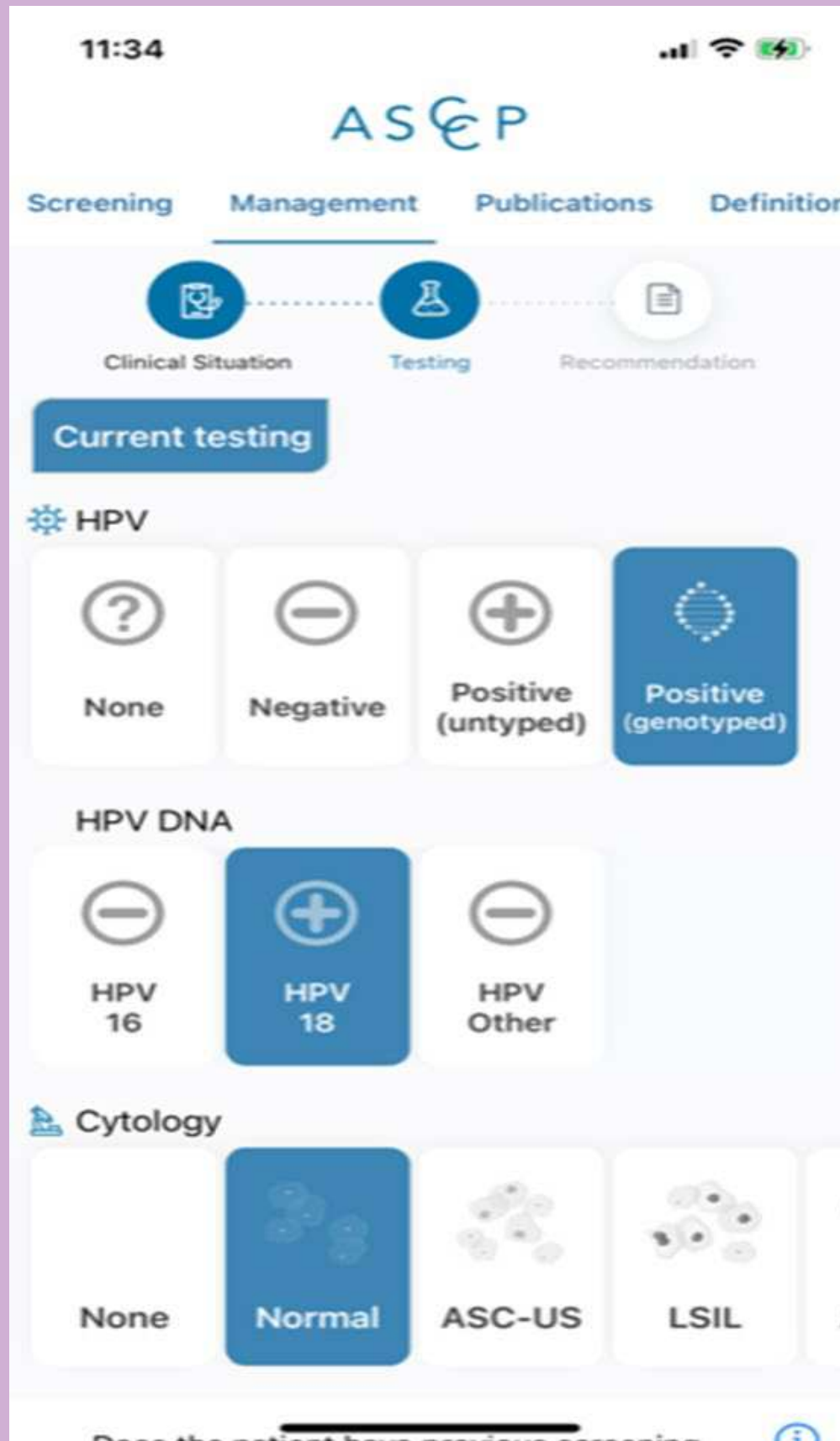
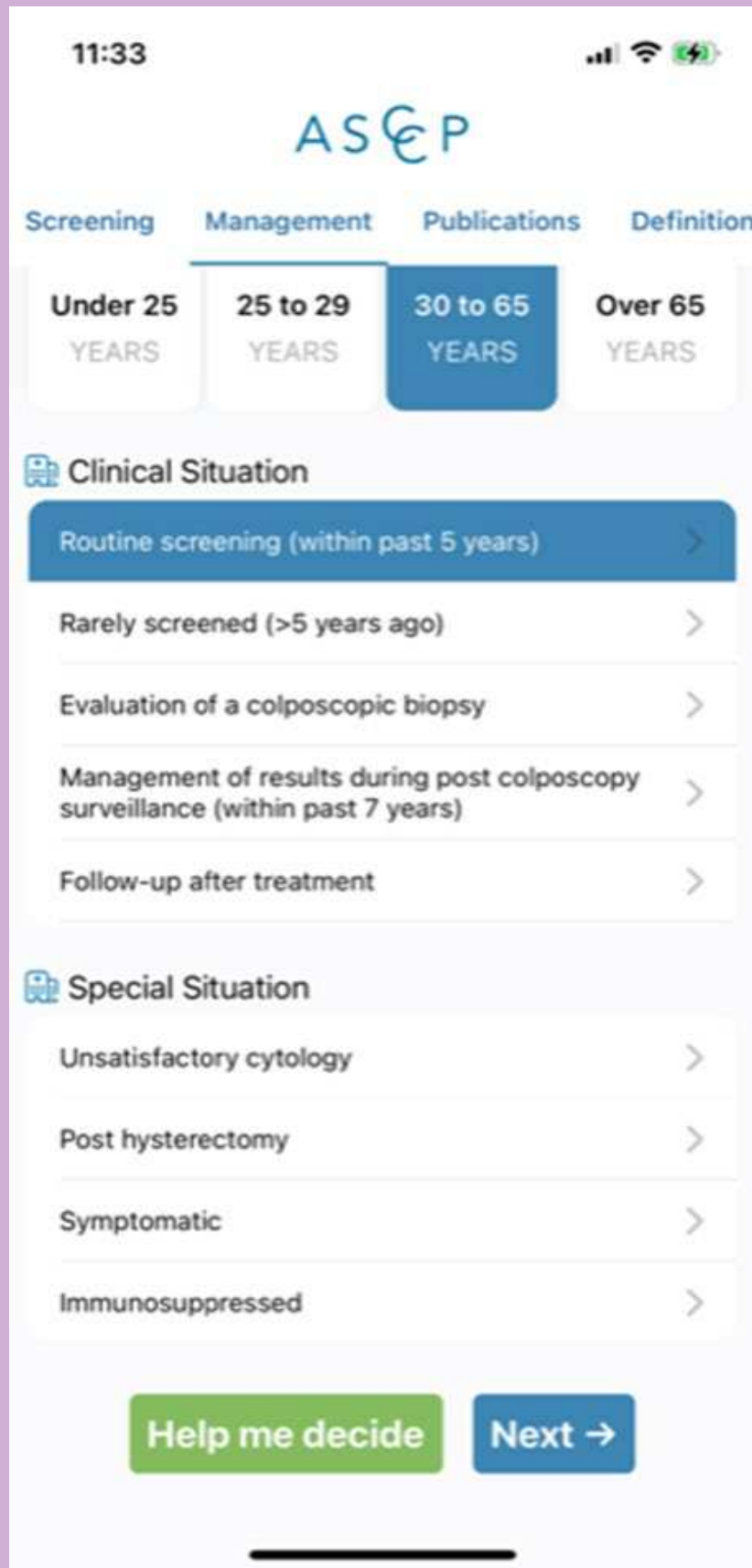
Recommendation updates based on new erratum publication.

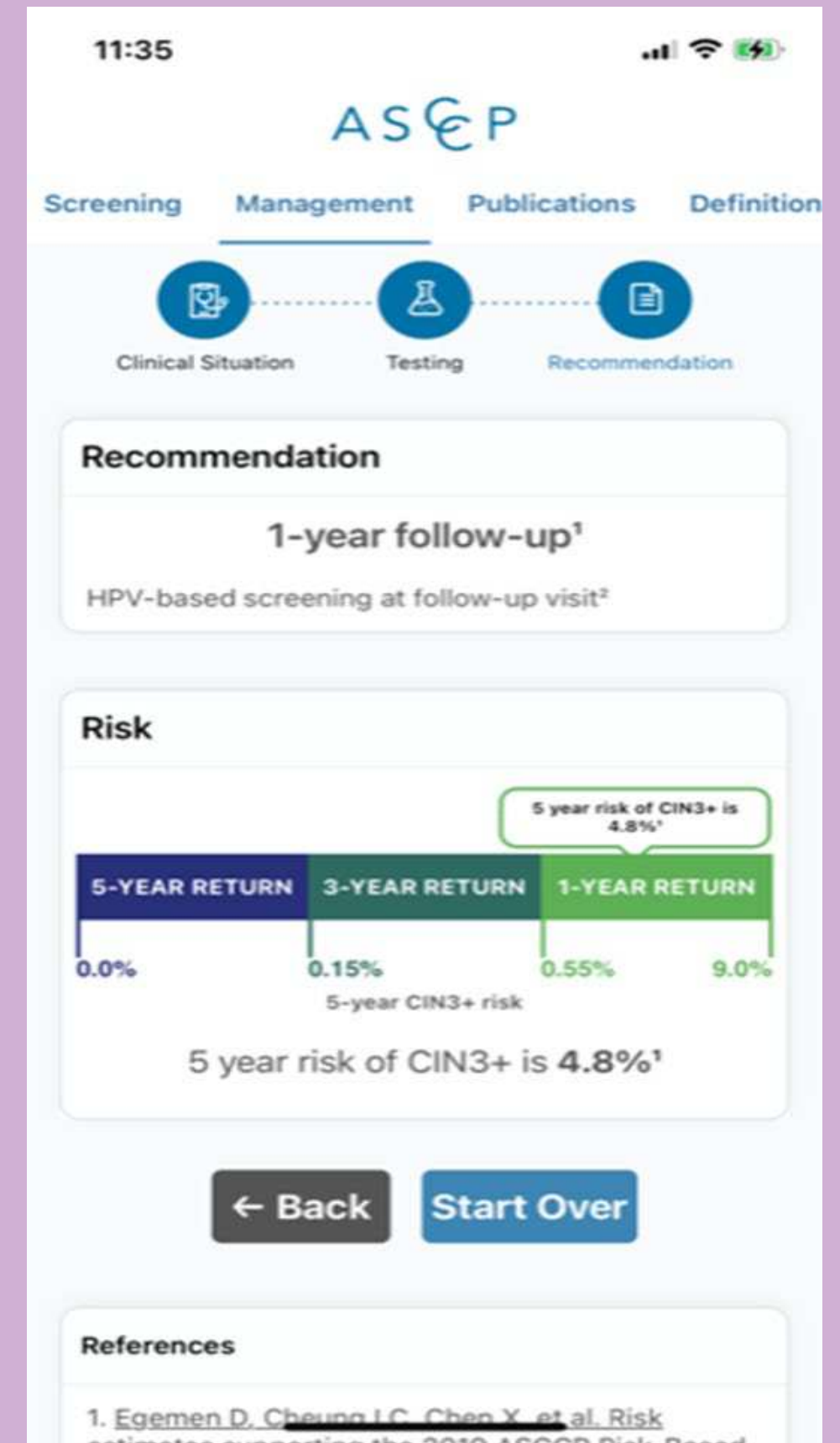
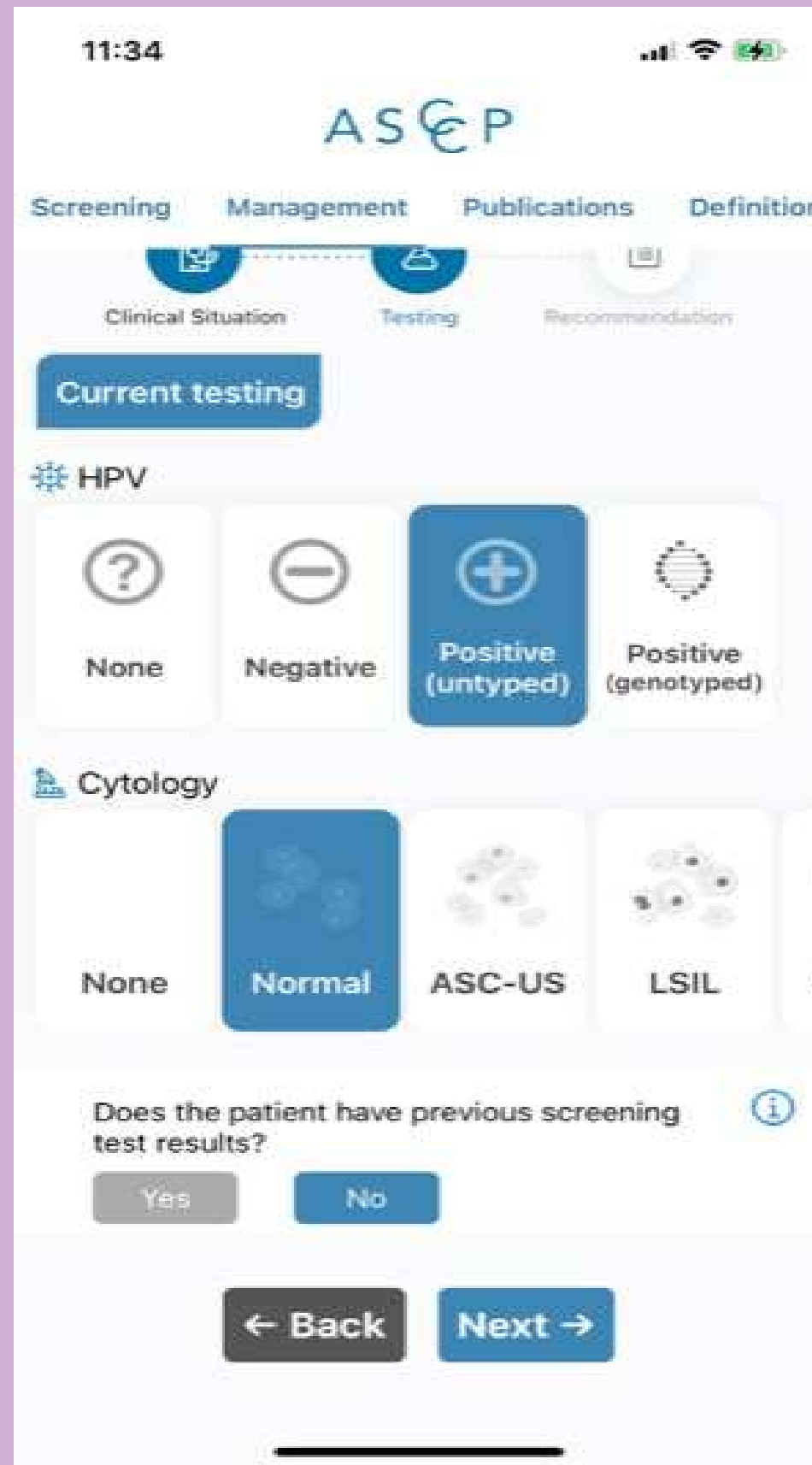
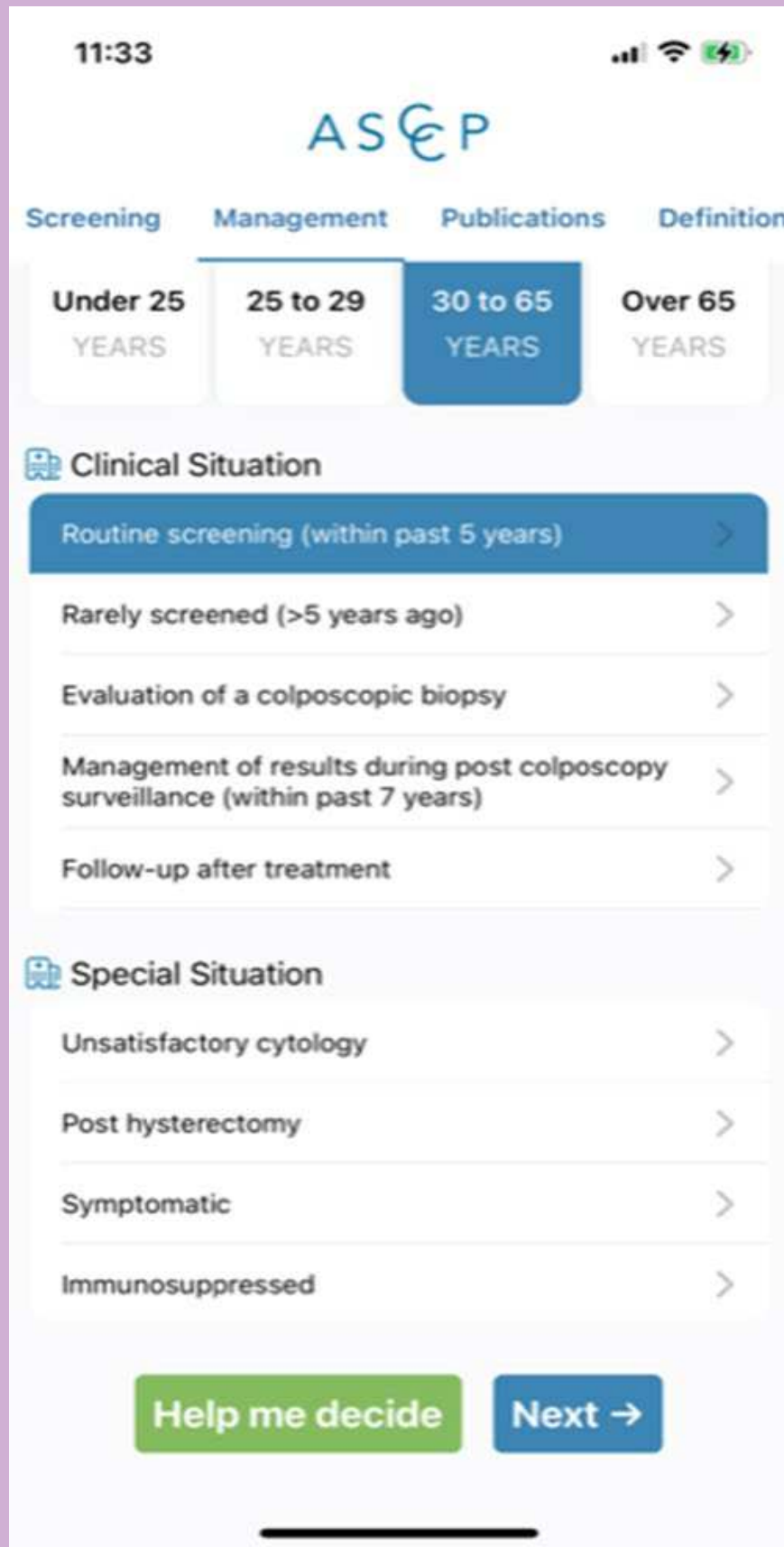
Preview



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Treatment

- Screening aims to identify high-grade precancerous cervical lesions to prevent progression to cervical cancer
- High-grade cervical lesions may be treated with excisional and ablative therapies
- Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy
- Treatment of precancerous lesions is less invasive than treatment of cancer

Poll Question

The highest rate of cervical adenocarcinoma (as opposed to squamous cell carcinoma) occurs in which group of women:

- A: Black
- B: American Indian/Alaskan Native
- C: Hispanic
- D: White Appalachian

Role of Race/Ethnicity, Geography on Cervical Cancer

- Increased cervical cancer mortality in black women
 - 10.1 deaths per 100,000 women (> 2X that of white women)
 - Higher mortality for older black women.
 - Similar screening rates vs white women but f/u and treatment differences
 - Higher rates of adenocarcinoma (worse prognosis than more common squamous cell carcinoma)

Role of Race/Ethnicity, Geography on Cervical Cancer

- Increased cervical cancer mortality in American Indian/Alaska Native women:
 - 3.2 deaths per 100,000 women
 - Lower screening rates (16.5% reported not receiving a Pap test in the past 5 years)
 - Inadequate follow-up
- Increased cervical cancer mortality in Hispanic women:
 - 2.6 deaths per 100,000 women [unadjusted for hysterectomy rate]
 - High rates occurring along the Texas-Mexico border
- Increased cervical cancer mortality in white living in geographically isolated and medically underserved areas (particularly Appalachia)
- Asian women have lower screening rates
 - Recently immigrated to the United States
 - Language or cultural barriers to screening

Role of Race/Ethnicity, Geography on Cervical Cancer

- Insurance coverage plays an important role
- Incidence of no pap smear in the last 5 years
 - 11.4% of the general population
 - 23.1% with no health insurance
 - 25.5% with no PCP
- No screening data for women with disabilities and those who identify as lesbian or transgender

Role of Race/Ethnicity, Geography on Cervical Cancer

- Progress in reducing cervical cancer incidence and mortality uneven
- Important contributing factors
 - Barriers to screening
 - Financial
 - Geographic
 - Language or cultural
 - Barriers to follow-up
 - Unequal treatment
 - Difference in cancer types

Additional Approaches to Prevention

Centers for Disease Control and Prevention's Advisory Committee on Immunization Practice (ACIP) recommends routine HPV vaccination

2-dose schedule for girls and boys who initiate the series at ages 9 to 14 years

3-dose schedule for girls and boys who initiate the series at ages 15 to 26 years and for immunocompromised

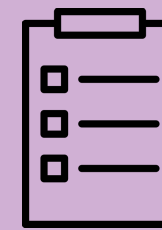
Shared decision making over age 27

- The overall effect of HPV vaccination on high-grade precancerous cervical lesions and cervical cancer is not yet known
- Possibility that vaccination might reduce the need for screening with cytology or hrHPV testing is not established.
 - Those vaccinated should continue screening as recommended until further evidence

What is to Come



In 2020, the American Cancer Society (ACS) recommend primary hrHPV testing as the preferred screening option for average-risk individuals aged 25–65 years



Cytology-based screening options are still included in the ACS guidelines in acknowledgement of barriers to widespread access and implementation, however, ACS strongly advocates phasing out cytology-based screening options in the near future



Although HPV self-sampling has the potential to greatly improve access to cervical cancer screening, and there is an increasing body of evidence to support its efficacy and utility, it is still investigational in the United States.

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Thank you!

Do you have any questions?